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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/426,038	10/25/99	VIND J	5579.210-US

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EXAMINER	
PONNALURI,P	
ART UNIT	**PAPER NUMBER**
1627	8

DATE MAILED: 03/01/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/426,038	Applicant(s) Vind
	Examiner P. Ponnaluri	Group Art Unit 1627

☒ Responsive to communication(s) filed on *Dec 6, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-22 and 27-29* is/are pending in the application.

Of the above, claim(s) *10, 22, and 27-29* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-9 and 11-21* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-22, 27-29 are currently pending in this application.

2. This application is a continuation in part of application 09/186,665, now abandoned.

3. Applicant's election of group I, claims 1-21; and species election of a) SEQ ID NO 1, b) polynucleotide sequences prepared by random mutagenesis, c) polynucleotide sequences encoding polypeptides, d) polypeptides are enzymes, e) enzymes are hydrolases, g) control sequence is a promoter, h) control sequence is a TAKA-amylase promoter, I) selectable marker provides biocide resistance (claim 9), k) pyrG, l) replication initiating sequence of group a), m) SEQ ID NO 1, n) modification is performed by DNA shuffling, and o) fungal cell is Aspergillus, in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Claims 22, 27-29 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Election was made **without** traverse in Paper No. 7.

5. Claims 10 and 19 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected species (applicants elected gene encodes a product which provides for resistance to biocide in claim 9; and library of polynucleotide sequences of interest is prepared by random mutagenesis in claim 2 which is different from the claimed method in claim 19). Election was made **without** traverse in Paper No. 7.

6. Claims 1-9, 11-18, 20-21 are currently being examined in this application.

7. In the specification page 1, applicants are requested to update the status of the parent application 09/186,665.

8. The use of the trademark QIAQUICK (in page 50, line 1), MIRACLOTH (page 50), SORVALL (page 50) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

9. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-9, 11-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims briefly recite a method of constructing and selecting a library of polynucleotide sequences of interest in filamentous fungal cells, comprising; a) transforming fungal cells with a population of DNA vectors, wherein each vector comprises a polynucleotide sequences encoding fungal selection marker and fungal replication initiating sequences; and a polynucleotide sequence of interest, b) cultivating the cells, c) selecting one or more transformants expressing a desired characteristics, d) isolating the transformants of interest.

The specification does not adequately provides a description of the replication initiating sequence having at least 50 % identity with the nucleic acid sequence of SEQ ID NO 1 or SEQ ID NO 2, or its respective functional subseqeunce thereof claimed by the instant claims; and a portion of receptor, a portion of antibody.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound; which requires a representative sample of compounds and/or a showing of

sufficient identifying characteristics; to demonstrate possession of the claimed generic(s). The specification merely describes specific polynucleotides, and the specification does not have support for antibody portion or enzyme portion or a portion of a receptor as claimed in claim 4. The specification does not sufficiently teach that the portion of the polypeptide would exhibit the same or similar property as the encode proteins. The specification does not sufficiently teach the replicating initiating sequence having at least 50 % identity with the nucleic acid sequence set forth in SEQ ID NO 1, or SEQ ID NO 2 or respective functional subsequence thereof.

12. Claims 1-9, 11-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for replication initiating sequence set forth in SEQ ID NO 1 or SEQ ID NO 2, does not reasonably provide enablement for replication initiating sequence with at least 50 % identity with SEQ ID NO 1 or SEQ ID NO 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (U.S.P.Q. 2d 1400 (CAFC (1988)). The factors to be considered include; the quantity of experimentation necessary, the amount of guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the predictability of the art and the breadth of claims.. The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount f direction or guidance presented.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. Besides the polynucleotides with the sequences SEQ ID NO:1 and SEQ ID NO:2, the specification fails to provide guidance as to how to make or use the replication initiating sequence with at least an 50% identity to SEQ ID NO1 or SEQ ID NO 2. The specification defines subseqeunce of SEQ ID NO 1 as being identical to the SEQ ID NO 1 sequence except that one or more nucleotides from the 5' and/or 3' end of the polynucleotides a sequence with SEQ ID NO 1 have been deleted, and the subseqeunce contains 100 to 2000 nucleotides (see page 15, lines 1-11). The specification discloses (page 13), that the degree of identity is determined by the computer programs known in the art such as GAP. However, the methods used by the applicant have not been disclosed and thus the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acid or amino acid sequences broadly encompassed by the claims due to the significant number of untaught sequences. Besides the specific nucleotide sequences disclosed in the specification (SEQ ID NO:1 and SEQ ID NO:2), the specification fails to provide guidance as to how to determine the open reading frame and non-coding sequences encompassed by the claims. The use of "percent" in conjunction with any of the various terms that refer to sequence similarity is a problem since sequence identity between two sequences has no common meaning within the art. The term "percent" can be defined by the algorithm and parameter values set when using the algorithm used to compare the sequences. The scoring of gaps when comparing one sequence to another introduces uncertainty as to the percent

of similarity between two sequences. Since the nucleic acid sequence of a polynucleotide determines its protein coding properties, predictability of which changes can be tolerated in a polynucleotide's nucleic acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which nucleic acids in the nucleotide sequence, if any are tolerant of modification and which are conserved (ie., expectedly intolerant to modification), and detailed knowledge of the ways in which the product's structure relates to its functional usefulness. However, the problem of predicting functional aspects of the product from mere sequence data of a single nucleic acid sequence and what changes can be tolerated is complex and well outside the realm of routine experimentation. Therefore, there is no evidence of record to show that one skilled in the art would be able to practice the invention as claimed without an undue amount of experimentation.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1-9, 11-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite by reciting a method of constructing and selecting or screening a library. From the claim language it is not clear whether the population of DNA vectors contain more than one variant of the polynucleotide sequence (whether the polynucleotide in a single DNA vector contains different variations, or a single variation DNA in each vector). Claim 1 recites 'selection pressure', clarification is requested what does applicants mean by selection pressure.

In claim 1 the recitation of polynucleotide sequence in step (I) is confusing since step (ii) recites polynucleotide sequence. Applicants are requested to clarify.

Claim 1 recites 'variant of polynucleotide', which is vague and indefinite. The specification does not have a definition for the variants. It is not clear which variants are included in this. Applicants are requested to clarify.

Claim 1 recites 'desired characteristic', clarification is requested what does applicants mean by desired characteristics. The specification does not recite a definition for the desired characteristic. Applicants are requested to clarify.

Claim 3 recites 'wherein the polynucleotide sequence encodes a polypeptide or is a control sequence; or wherein the polynucleotide sequence encodes a polypeptide or part thereof and further comprises a control sequence involved in the expression of the polypeptide or a part of

such control sequence.' it is not clear which polynucleotide sequence encodes which polypeptide. Does applicants mean that the polynucleotide sequence of step (I) or the polynucleotide sequence as in step (ii). Claim 3 is also indefinite by reciting 'a polypeptide or a part thereof, or further comprising a control sequence or part of control sequence. It is not clear which part is included and the size of the part and which control sequence and which part of the control sequence. The specification does not disclose part of the polypeptide or part of the control sequence.

Claim 4 recites 'a portion thereof', clarification is requested which portion applicants are referring to. The portion of the enzyme or receptor or antibody has any specific function or structure. The specification disclosure does not have nay definition for the portion thereof.

Claim 7 recites the limitation "the control sequence" in line 1. There is insufficient antecedent basis for this limitation in the claim or in claim 1.

Claim 9 recites the limitation "the selective marker" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim or in claim 1.

Claim 9 recites 'genes which encode a product which provides for resistance to biocide or viral toxicity..', clarification is requested what does applicants mean by provides for resistance to ..., does applicants mean that the gene encodes a products which is responsible for resistance to biocide.

Claim 9 is indefinite by reciting improper Markush group. Applicants are requested to amend the claim by deleting "or" before 'prototrophy'.

Claims 12-16 are indefinite by recitation of "% identity. The use of such terms as percent homology, percent similarity, and percent identity in connection with nucleic acid sequence is vague and indefinite in the absence of a clear description or definition of what the term means. This is because sequence identity between two sequences has no common meaning within the art. Although the methods for determining identity between two sequences, such as the use of programs like BLAST, BLASTIN, or FAST, as disclosed on page 13, and the disclosure do not adequately describe how the applicants themselves determined the percent identity. The disclosure does not allow one skilled in the art to determine the existence of gaps, or which mismatches, alterations or mutations are encompassed by the claims. It is therefore unclear what isolated sequences the applicants claim.

Claim 17 recites ' a respective functional subseqeunce thereof', clarification is requested what does applicants mean by functional subseqeunce thereof. The specification does not recite which subseqeunce is functional subseqeunce. The specification does not recite which function and how the subseqeunce is different from the SEQ ID NO 1 or SEQ ID NO 2.

Claim 18 recites the limitation "wherein the modification of parent polynucleotide sequence " in lines 1-2. There is insufficient antecedent basis for this limitation in the claim or in claim 2.

Claim 18 recites 'preferably' which is indefinite. Applicants are requested to clarify.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-9, 18-21 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 98/01470 (Christensen).

Christensen discloses that a transcription factor regulating alpha amylase promoter initiated expression in filamentous fungi, especially in Aspergilli, (refers to instant claim 20) DNA sequences encoding for said factor, its transformation into and expression in fungal host organisms, and the use of said factor (see the abstract). The reference discloses a method of producing a filamentous fungal cell comprising the introduction of a DNA fragment coding for any such factor in to a filamentous fungus, wherein alpha amylase promoter or a co-regulator promoter regulates the expression of a polypeptide of interest in a manner whereby said promoter will be expressed in said fungus (see pages 3-4) (refers to instant claim 1). The reference discloses that DNA sequence encoding transcription factor homologous to the transcription factor of the invention, the DNA sequences may be derived by similar screening of cDNA library of another microorganism. The reference discloses that the method of producing a filamentous fungal host cell comprising the introduction of any of the DNA fragments into a filamentous fungus wherein the alpha amylase promoter or another coregulated promoter regulates the

expression of a polypeptide of interest in a manner whereby said factor will be expresses in said fungus (see page 12, lines 29-34). The reference discloses that the invention provides a recombinant expression vector comprising DNA construct of the invention (see page 13, lines 4-5). The reference discloses the promoters for use in filamentous fungal cells (see pages 13-14) (refers to instant claim 8). The reference discloses a method of producing a polypeptide of interest, whereby a host cell is grown under conditions conductive to the production of said factor and said polypeptide of interest, and the polypeptide of interest is recovered (see page 15) (refers to instant claim 1, steps b and c). The reference discloses that the method may also be used for production of industrial enzymes such as hydrolases (see page 15) (refers to instant claim 4-5), and proteases (see page 16, line 1) (refers to instant claim 6). The reference teaches that the transcription factor is used to identify the sequences which bind to alpha amylase promoter to which it binds, by using GST fusion protein (refers to selection marker of the instant claims). The reference clearly anticipates the claimed invention.

17. No claims are allowed.

Any inquiry concerning this communication should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached at (703)308-2439. The fax number for this group is (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703)308-0196.

P. Ponnaluri
Patent Examiner
Technology center 1600
Art Unit 1627
26 February 2001